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LONGITUDINAL SYMPTOM COURSE IN ADULTS WITH RECURRENT DEPRESSION: IMPACT ON IMPAIRMENT AND RISK OF PSYCHOPATHOLOGY IN OFFSPRING

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ABSTRACT

Background: Major depressive disorder (MDD) is common and is associated with an increased risk of psychopathology in offspring. However, depression shows considerable heterogeneity in its course over time. The aim of this study was to examine the relationship between parent depression symptom trajectories and i) quality of life and social impairment and ii) psychiatric disorder and depression symptoms in their offspring.

Method: Participants were from a longitudinal study of 337 parents with recurrent MDD and their adolescent offspring. Families were assessed on three occasions over four years. Parent depressive symptoms and current MDD diagnosis were assessed using the Schedules for Clinical Assessment in Neuropsychiatry. Adult quality of life and social impairment were derived from the EuroQol and current employment status. Psychiatric outcomes in offspring were assessed using the Child and Adolescent Psychiatric Assessment.

Results: Using latent class growth analysis, three distinct classes of parental depression symptoms were identified (asymptomatic, mild, and chronic high) Parent depression classes were associated with their own quality of life and social impairment, and with psychiatric disorder and depression symptoms in their offspring.

Limitations: i) We were unable to test associations with specific offspring disorders, ii) we did not address the direction of effects underlying associations, iii) the sample consisted primarily of mothers and findings may not generalise to depressed fathers.

Conclusion: Longitudinal assessments of depressive symptoms in parents could help identify families who are most in need of early intervention.

Keywords: Adolescent; Depression: Parent; Symptom course; Longitudinal

INTRODUCTION

Major depressive disorder (MDD) is a serious and increasing global health issue, resulting in substantial costs to individuals, families and society (Murray and Lopez, 1997; Thapar et al., 2012). Parental depression is common and is a key risk factor for youth psychiatric disorder, with offspring of depressed parents showing an increased risk of depression, anxiety and disruptive behaviour disorders when compared with controls (Beardselee et al., 1998; Mars et al., 2012; Weissman et al., 2006). Depression when its onset is in adolescence is especially problematic given high rates of recurrence into adulthood, challenges with treatment and associated impairments including an increased risk of suicide (Thapar et al., 2012). Prevention of depression and other psychiatric disorders in adolescence is therefore a priority, especially in high-risk populations (National Research Council and Institute of Medicine, 2009).

The offspring of parents with depression are a potentially important target group for early intervention and prevention, however, not all young people with a depressed parent go on to develop such problems. Depression is very heterogeneous (Hammen and Brennan, 2003; Mars et al., 2012) and this may partly explain differences in child outcomes. For example, parental clinical illness features such as early age of onset, chronicity, severity, and specific depression symptoms have all been found to be associated with child outcomes (Foster et al., 2008; Hammen and Brennan, 2003; Klein et al., 2005; Mars et al., 2012; Mars et al., 2013; Weissman et al., 1984). Longitudinal studies highlight that the natural course of depression, like many common health problems is highly variable over time (Judd and Akiskal, 2000; Judd et al., 1998; Nandi et al., 2009). Indeed it is well established that some individuals with depression experience residual depression symptoms and associated impairment in-between episodes, whilst others show complete remission for substantial periods (Judd and Akiskal, 2000; Judd et al., 1998; Nierenberg et al., 2010). The importance of depression heterogeneity, as defined by course variability, in child-rearing adults with a history of recurrent depressive disorder is not known; either in relation to the impact on parent quality of life and impairment or in terms of offspring risk of psychopathology.

The present investigation utilises data from a longitudinal three-wave study of families where one parent had at least two prior episodes of DSM-IV MDD during their lifetime, confirmed at interview. The first aim was to identify distinct classes of parent depression, based on their depression symptom levels at each of the three assessment time points, and validate these classes by showing associations with clinical features that index depression severity. The second aim was to examine the impact of parent depression symptom classes on adult quality of life and social impairment. The third aim was to examine the relationship between parent depression symptom classes and risk for psychiatric disorder and depression symptoms in adolescent offspring.

METHODS

Sample

Data were drawn from the Early Prediction of Adolescent Depression (EPAD) study: a prospective longitudinal study of the high-risk offspring of recurrently depressed parents (Mars et al., 2012). Families were recruited predominantly from primary care practices across south Wales, UK (78%). Remaining families were recruited from a sample with previously identified unipolar depression (19%) and community volunteers (3%). Parents with a history of psychotic disorder or bipolar disorder or those who met DSM-IV criteria for mania/hypomania were excluded. There were no diagnostic exclusion criteria for the children in the study, although the participating child was required to have an IQ $\geq$ 50.

The eligible baseline sample included 337 parents with recurrent unipolar depression (315 mothers and 22 fathers; age 26-55 years, mean 41.7 years) and their adolescent offspring (197 females and 140 males; age 9-17 years, mean 12.4 years). Parental history of recurrent unipolar depression was confirmed at interview (two or more lifetime MDD episodes); however, parents need not have been depressed at the time of recruitment.

Families were assessed at three time points between April 2007 and April 2011. The average time between the baseline assessment and first follow-up was 16.2 months (SD 2.69) and between the first and second follow-ups was 12.5 months (SD 1.56). Two families were excluded at follow-up as the affected parent received a clinician diagnosis of bipolar affective disorder. The present investigation focuses on the 233 families (70% of baseline eligible sample) with complete interview data at each of the three time points. Families with missing data had higher baseline parent depression scores ($t(314) = -2.96$, $p=.003$), but there were no differences in terms of baseline child depression symptoms ($t(331) = -1.45$, $p=.155$).

The Multi-Centre Research Ethics Committee for Wales reviewed and approved the study protocol. Written informed consent/assent was obtained from each participant at each of the three

assessments. More detailed information about study recruitment, sample characteristics and assessment procedures has been reported previously (Mars et al., 2012).

Measures

Child DSM-IV psychiatric disorder: The Child and Adolescent Psychiatric Assessment (CAPA), parent and child versions (Angold and Costello, 2000) is a semi-structured diagnostic interview which was used at each assessment to assess DSM-IV psychiatric disorder, based on symptoms and impairment during the preceding 3 months. Parent and child reported diagnoses were combined (using an either/or approach) at each time point to generate an overall DSM-IV diagnosis occurring over the study. The DSM-IV disorders assessed included mood disorders, anxiety disorders, disruptive behaviour disorders, eating disorders and ADHD. All cases meeting criteria for diagnosis, together with all sub-threshold cases, were reviewed by two child and adolescent psychiatrists (AT and RP). The CAPA was also used to generate a parent/child-combined symptom count of DSM-IV depression symptoms (maximum 9) at the final follow-up. A symptom was considered present if reported by either the parent or the child at interview. Mean imputation was used where there was one missing symptom.

Parent depression symptoms: The Schedules for Clinical Assessment in Neuropsychiatry (SCAN) (Wing et al., 1990) diagnostic interview was used at each assessment to assess the number of DSM-IV depression symptoms occurring over the previous month (maximum 9 symptoms). The total number of past month depression symptoms at each time point was collapsed into five groups (to help estimation due to small cell counts) and used to generate the parent depression symptom trajectories (see below). Assessments and diagnoses were reviewed by an experienced adult psychiatrist (DS).

Parent depression - clinical features: Age of depression onset and presence of a severe past depressive episode (defined as Global Assessment of Functioning score (American Psychiatric Association, 1994) less than 30 or hospitalisation for depression (Mars et al., 2012)) were ascertained at baseline from a timeline of the parent's previous depressive episodes. The timeline was generated using a life history calendar approach (Belli, 1998; Caspi et al., 1996). Information about current depression treatment (medication and psychotherapy) was obtained at each time-point.

Parent health and social impairment: A measure of quality of life/current health impairment was derived from the EuroQol 5D 3L questionnaire (The EuroQol Group, 1990) at each assessment. This asks about level of problems related to mobility, self care, usual activities, pain/discomfort and level of anxiety/depression. Response categories are "no difficulty", "some difficulty", and "a lot of difficulty" (scored as 0, 1 and 2 respectively). The "quality of life/health impairment" score was derived from the totals with the anxiety/depression score omitted from the total score. The parents' current employment status was ascertained by questionnaire report on each occasion and used as a measure of social impairment.

Analysis

Latent class growth analysis (LCGA) (Nagin, 2005) was used to identify distinct patterns of depression symptoms in parents over time using depression scores derived from the SCAN at each of the three time points of the study. In LCGA, homogenous classes are identified based on specific growth parameters describing each parent's initial level and rate of change in depression symptoms. Each parent is then given a probability of belonging to each class. In contrast to growth mixture modeling (GMM), LCGA assumes no within class variance on the growth factors (the intercept and slope) hence it is a popular choice for the analysis of binary or ordinal data, when within-class growth-factor distributions would be unlikely to be normally distributed.

In the current analyses, parameter constraints were employed in order to create a group who were asymptomatic throughout the time period of study. This class would serve as the comparison group for the analyses that followed. Due to the probabilistic nature of the mixture model, this class does not simply contain all individuals who reported zero symptoms at each time point; however individuals with this symptom profile would have a very high probability of being assigned to this class.

A series of models were fitted and theoretical and statistical steps were taken to decide which model provided the best fit to the data. These included a number of fit statistics (including the Bayesian information criterion (BIC), Bootstrap Likelihood Ratio Test (BLRT) and entropy values). From previous literature (Barker, 2013; Campbell et al., 2007; Campbell et al., 2009; Skipstein et al., 2010) we expected to find at least three classes of parental depression symptoms, therefore models containing up to five classes were estimated (Supplementary Table 1). Due to estimation problems with the five-class model statistics for this model are not shown.

Following the identification of a mixture model which adequately described the longitudinal pattern of symptoms, a number of distal outcome models were estimated. These examined the relationship between parent depression symptom classes and i) parental clinical features (used to validate the classes; age of onset, history of severe depression and depression treatment), ii) parent health and social impairment (health related quality of life and unemployment), and iii) offspring psychiatric disorder and depression symptoms.

Depending on the goal of each analysis, either a one-step or bias-adjusted three-step model (Vermunt, 2010) was estimated. Both approaches would allow for the uncertainty related to latent class membership, however the latter routine, in which any outcomes or covariates do not impact on the latent class measurement model, was deemed more appropriate for the analysis seeking to validate the latent class grouping. Analyses were conducted using Mplus version 7(Muthén and Muthén).

RESULTS

Table 1 presents demographic information, clinical information regarding the index parent's depression, and prevalence of offspring DSM-IV psychiatric disorders at each time point of the study. All of the index parents in the sample had a history of recurrent depression confirmed at interview (at least two lifetime episodes of MDD); however parents were not necessarily depressed at the time of recruitment. Of the 233 parents with complete information at each of the three study time points, 33.3% (n=77) experienced an episode of DSM-IV MDD at one or more assessments of the study. In line with previous family studies (Weissman et al., 2006), rates of offspring psychiatric disorder were elevated in this sample when compared with normative data from a UK epidemiological survey of children aged 11–15 years (Green, 2005).

Latent classes of parental depression symptoms

Based on fit statistics, size of latent classes and parsimony, a three class model represented the best fit to the data (Supplementary Table 1). Lower BIC values reflect superior fit of a given model and the BLRT also supported this model. The identified classes reflected asymptomatic, mild and chronic high depression symptoms (Figure 1 and Supplementary Figure 1). The most common depression class was characterised by mild depression symptoms (67% of sample). Twenty one percent of parents were in the chronic high symptoms class and 12% were in the asymptomatic class. In all further analyses the asymptomatic class is treated as the reference group. Table 2 presents demographic information according to parent depression symptom class.

There was evidence to suggest differences between the parent depression symptom classes with regards to clinical features of their illness (age of onset, history of severe depression and depression treatment) (Table 3). As expected, there was an increase in the severity of clinical features with increasing severity of parental depression symptom class. For example, the proportion of parents

who had taken antidepressant medication during the study was 49% in the asymptomatic class, 70% in the mild class and 89% in the chronic high class.

Relationship between parent depression symptom classes and adult quality of life and social impairment

There was evidence that quality of life (health related) and social impairment (indexed via unemployment) differed across parental depression classes (Table 3). Relative to the asymptomatic group of parents, the chronic-high class had poorer quality of life scores (2.9 vs 0.5; mean difference 2.4, 95% CI 1.55 to 3.28) and a greater prevalence of unemployment (49.8% vs 7.8%; risk difference 42.0%, 95%CI 20.8% to 63.2%). Levels of health and social impairment were similar amongst parents in the asymptomatic and mild classes.

Relationship between parent depression symptom classes and offspring psychopathology

1) Offspring DSM-IV psychiatric disorder: In total, 40% *(*n=93) of offspring met criteria for a DSM-IV psychiatric disorder on at least one occasion; approximately two thirds of adolescents with a disorder had a parent who was in the group characterised by mild parental depression symptoms. The prevalence of offspring psychiatric disorder differed across the parent depression classes. As shown in Table 4, the prevalence of offspring DSM-IV disorder was higher in the mild and chronic high symptom classes than in the asymptomatic class (prevalence of disorder: 5.7% in asymptomatic class; 40.2% in the mild symptoms class (risk difference 34.5%, 95% CI 14.1% to 54.9%) and 57.4% in chronic high symptoms class (risk difference 51.7%, 95% CI 28.0% to 54.9%)).

The prevalence of specific offspring disorders (mood disorders, disruptive behaviour disorders and anxiety disorders) by parent depression symptom class is shown in Table 4. Analyses were exploratory due to small cell sizes. Nevertheless, there was evidence to suggest differences between the parent classes with regards to offspring mood disorder and anxiety disorder but not for disruptive behaviour disorder.

2) Offspring DSM-IV depression symptoms:

There was evidence that offspring depression symptoms at final follow-up differed across the parent depression symptom classes. As shown in Table 5, the mean number of DSM-IV depression symptoms was higher amongst offspring of parents in the mild symptoms class and the chronic high symptoms class than the asymptomatic class (minimal symptoms class: 1.92 vs 0.99, mean difference 0.93, 95% CI 0.36 to 1.50; chronic high symptoms class: 2.50 vs 0.99, mean difference 1.51, 95% CI 0.64 to 2.38).

DISCUSSION

This study is, as far as we are aware, the first to examine the relationship between parent depression symptom course and adolescent psychiatric disorder amongst offspring of parents with recurrent depression (at least two episodes of MDD). Differences were found between the parent depression symptom classes with regards to their own health-related quality of life and social impairment (indexed via unemployment), and with psychiatric disorder and depression symptoms in their adolescent children. The prevalence of psychiatric disorder and the mean number of depression symptoms were elevated amongst offspring in the mild and chronic high classes when compared to the asymptomatic class, suggesting that even minimal levels of depression symptoms in parents across time are associated with increased risk for psychopathology in offspring. Indeed, approximately two thirds of the adolescents with a psychiatric disorder were in the subgroup characterised by mild parental depression symptoms. These findings highlight the impact of continued sub-threshold symptoms of depression on offspring mental health outcomes.

Three distinct classes of parental depression symptoms were identified in the present study. These classes were characterised by stable levels of depression symptoms that differed in the level of severity (asymptomatic, mild and chronic high).The depression symptom classes we identified are broadly consistent with previous research; other studies that have examined adult depression trajectories have also identified a small class of mothers with chronic high depression symptoms and a number of other classes of mothers showing stable symptoms across time that differ in level of severity (Barker, 2013; Campbell et al., 2007; Cents et al., 2013; Skipstein et al., 2010). Fewer studies, however, have identified groups with increasing or decreasing symptoms over time (Campbell et al., 2009; Skipstein et al., 2010). It is possible that a longer time span of assessment is required in order for such trajectory classes to emerge. We are not aware of any studies that have investigated variations in symptom course amongst those with recurrent depression specifically, or examined cross-generational links between parent symptom course and risk for psychiatric disorder

in adolescence. We have demonstrated that there is substantial heterogeneity in illness course amongst a sample of adults with recurrent MDD. These patterns in variation would not easily be identifiable from cross-sectional assessment, but have implications in terms of impact on offspring. The longitudinal symptom classes we derived differed with regards to parental impairment and clinical depression features (including age of depression onset, severe depression, and treatment for depression). It is interesting to note there was little evidence of differences in impairment between parents in the mild and the asymptomatic classes, but the offspring of adults with mild symptoms had a substantially increased risk of psychopathology.

The few existing studies that have examined adolescent outcomes in relation to parent symptom course have been conducted in community samples of adults, where the majority of parents report subclinical levels of depression symptoms. Studies have also typically focused on offspring psychological and behavioural symptoms rather than psychiatric disorder. For example, Campbell et al (2009) identified five subgroups of maternal depression course in a population sample of 1300 families, and found that chronic maternal depression symptoms occurring at varying levels of severity were associated with greater internalising symptoms, depression symptoms and loneliness scores in their adolescent children, compared to offspring of never-depressed mothers. In another study of 289 adolescent boys, Gross et al (2009) found higher levels of maternal depressive symptoms to be associated with externalising but not internalising symptoms.

Strengths and limitations

The main strengths of the study include a large sample size for a study of this kind, the longitudinal design, the comprehensive assessments of parent and child psychopathology, and good follow up rates. However, results must also be interpreted in light of several limitations. First, the number of children in the sample with specific psychiatric disorders (particularly mood disorders) was relatively small and this may have reduced power to detect differences between the parent symptom classes when focusing on particular adolescent disorders. However, to date, this is the largest longitudinal

family study of offspring of parents with recurrent depressive disorder, and diagnoses were established rigorously. Second, this paper did not address the direction of effects underlying intergenerational associations. It is possible that psychiatric disorder and depression symptoms in children may exacerbate problems in their parents. Third, the majority of parents in our sample were mothers recruited from primary care, and caution is required in generalising findings to children of depressed fathers or to samples that do not have a history of recurrent depression. It is possible that associations between parental depression and offspring psychopathology may be different for mothers and fathers. Sensitivity analyses removing the 19 fathers from the analyses did not change the pattern of results. Fourth, the analysis is based on data at three time points with little information about symptoms in-between assessments, and this may have affected the depression classes generated. Finally, as not all of the children in the sample had passed through the peak risk period for the onset of psychopathology by the final assessment, it is likely that some children may go on to develop depressive or other disorders in the future.

Summary and implications

Depression is a heterogeneous disorder and some aspects of this heterogeneity can be captured by identifying sub-groups defined by the pattern of symptoms over time. We have shown that, within a sample of parents with a history of recurrent depression, multiple distinct symptom classes can be identified and that these depression classes are related not only to parental quality of life and social impairment, but also psychiatric disorder and depression symptoms in their adolescent children. Our findings highlight the need to follow up and monitor depression symptoms in parents with recurrent depression over time. For those with any level of persisting symptoms, the impact on their own quality of life and social impairment, and the possibility of psychiatric disorders, including depression in their children needs to be considered.

CONTRIBUTIONS

Conception and design of the study: BM, SC, FR, GTH, DS, NC, AKT, AT; Organisation of the conduct of the study: BM, SC, AT; Carrying out the study (including acquisition of study data): BM, SC, DS, RBJ, RS, GH, RB, AT. Analysis of study data: BM, JH; Interpretation of study data: BM, SC, FR, GTH, DS, RBJ, RS, GH, RB, NC, AKT, JH, AT; Draft the output: BM; Critique the output for important intellectual content: BM, SC, FR, GTH, DS, RBJ, RS, GH, RB, NC, AKT, JH, AT. All authors have contributed to and have approved the final manuscript.

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CONFLICT OF INTEREST

None of the authors report any conflict of interests.

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HIGHLIGHTS

- We identified three distinct parent depression symptom classes
- The identified classes reflected asymptomatic, mild and chronic high depression symptoms
- Parent depression classes were associated with their own health and social impairment
- Parent depression classes were associated with psychopathology in their offspring
- Even minimal parent symptoms over time were associated with increased offspring risk

REFERENCES

American Psychiatric Association, 1994. Diagnostic and statistical manual of mental disorders 4th ed. Washington. DC.

Angold, A., Costello, E.J., 2000. The Child and Adolescent Psychiatric Assessment (CAPA). Journal of the American Academy of Child & Adolescent Psychiatry 39, 39-48.

Barker, E.D., 2013. The duration and timing of maternal depression as a moderator of the relationship between dependent interpersonal stress, contextual risk and early child dysregulation. Psychological Medicine. 43, 1587-1596.

Beardselee, W.R., Versage, E.M., Gladstone, T.R., 1998. Children of affectively ill parents: A review of the past 10 years. Journal of the American Academy of Child & Adolescent Psychiatry 37, 1134-1141.

Belli, R.F., 1998. The structure of autobiographical memory and the event history calendar: potential improvements in the quality of retrospective reports in surveys. Memory 6, 383-406.

Campbell, S.B., Matestic, P., von Stauffenberg, C., Mohan, R., Kirchner, T., 2007. Trajectories of maternal depressive symptoms, maternal sensitivity, and children's functioning at school entry. Developmental Psychology 43, 1202.

Campbell, S.B., Morgan-Lopez, A.A., Cox, M.J., McLoyd, V.C., 2009. A latent class analysis of maternal depressive symptoms over 12 years and offspring adjustment in adolescence. Journal of Abnormal Psychology 118, 479.

Caspi, A., Moffitt, T.E., Thornton, A., Freedman, D., Amell, J.W., Harrington, H., Smeijers, J., Silva, P.A., 1996. The life history calendar: A research and clinical assessment method for collecting retrospective event-history data. International Journal of Methods in Psychiatric Research 6, 101-114.

Cents, R., Diamantopoulou, S., Hudziak, J., Jaddoe, V., Hofman, A., Verhulst, F., Lambregtse-van den Berg, M., Tiemeier, H., 2013. Trajectories of maternal depressive symptoms predict child problem behaviour: The Generation R Study. Psychological Medicine 43, 13-25.

Foster, C.E., Webster, M.C., Weissman, M.M., Pilowsky, D.J., Wickramaratne, P.J., Rush, A.J., Hughes, C.W., Garber, J., Malloy, E., Cerda, G., 2008. Course and severity of maternal depression: Associations with family functioning and child adjustment. Journal of Youth and Adolescence 37, 906-916.

Green, H., 2005. Mental health of children and young people in Great Britain, 2004. Palgrave Macmillan Basingstoke.

Gross, H.E., Shaw, D.S., Burwell, R.A., Nagin, D.S., 2009. Transactional processes in child disruptive behavior and maternal depression: A longitudinal study from early childhood to adolescence. Development and Psychopathology 21, 139-156.

Hammen, C., Brennan, P.A., 2003. Severity, chronicity, and timing of maternal depression and risk for adolescent offspring diagnoses in a community sample. Archives of General Psychiatry 60, 253-258.

Judd, L., Akiskal, H., 2000. Delineating the longitudinal structure of depressive illness: beyond clinical subtypes and duration thresholds. Pharmacopsychiatry.

Judd, L.L., Akiskal, H.S., Maser, J.D., Zeller, P.J., Endicott, J., Coryell, W., Paulus, M.P., Kunovac, J.L., Leon, A.C., Mueller, T.I., 1998. A prospective 12-year study of subsyndromal and syndromal depressive symptoms in unipolar major depressive disorders. Archives of General Psychiatry 55, 694-700.

Klein, D.N., Lewinsohn, P.M., Rohde, P., Seeley, J.R., Olino, T.M., 2005. Psychopathology in the adolescent and young adult offspring of a community sample of mothers and fathers with major depression. Psychological Medicine 35, 353-365.

Mars, B., Collishaw, S., Smith, D., Thapar, A., Potter, R., Sellers, R., Harold, G.T., Craddock, N., Rice, F., Thapar, A., 2012. Offspring of parents with recurrent depression: which features of parent depression index risk for offspring psychopathology? Journal of Affective Disorders 136, 44-53.

Mars, B., Harold, G.T., Elam, K.K., Sellers, R., Owen, M.J., Craddock, N., Thapar, A.K., Rice, F., Collishaw, S., Thapar, A., 2013. Specific parental depression symptoms as risk markers for new-onset depression in high-risk offspring. Journal of Clinical Psychiatry. 74, 925-931. doi: 910.4088/JCP.4012m08152.

Murray, C.J., Lopez, A.D., 1997. Alternative projections of mortality and disability by cause 1990-2020: Global Burden of Disease Study. Lancet 349, 1498-1504.

Muthén, L.K., Muthén, B.O., 1998-2012. Mplus User ' s Guide (7th edition), Los Angeles.

Nandi, A., Beard, J.R., Galea, S., 2009. Epidemiologic heterogeneity of common mood and anxiety disorders over the lifecourse in the general population: a systematic review. BMC Psychiatry 9, 31.

National Research Council, Institute of Medicine, 2009. Depression in Parents, Parenting, and Children: Opportunities to Improve Identification, Treatment, and Prevention. The National Academies Press, Washington, DC.

Nierenberg, A., Husain, M., Trivedi, M., Fava, M., Warden, D., Wisniewski, S., Miyahara, S., Rush, A., 2010. Residual symptoms after remission of major depressive disorder with citalopram and risk of relapse: a STAR* D report. Psychological Medicine 40, 41.

Skipstein, A., Janson, H., Stoolmiller, M., Mathiesen, K.S., 2010. Trajectories of maternal symptoms of anxiety and depression. A 13-year longitudinal study of a population-based sample. BMC Public Health 10, 589.

Thapar, A., Collishaw, S., Pine, D.S., Thapar, A.K., 2012. Depression in adolescence. Lancet.

The EuroQol Group, 1990. EuroQol-a new facility for the measurement of health-related quality of life. Health Policy 16, 199-208.

Vermunt, J.K., 2010. Latent class modeling with covariates: Two improved three-step approaches. Political Analysis 18, 450-469.

Weissman, M., Wickramaratne, P., Nomura, Y., Warner, V., Pilowsky, D., Verdeli, H., 2006. Offspring of depressed parents: 20 years later. American Journal of Psychiatry 163, 1001-1008.

Weissman, M.M., Wickramaratne, P., Merikangas, K.R., Leckman, J.F., Prusoff, B.A., Caruso, K.A., Kidd, K.K., Gammon, G.D., 1984. Onset of major depression in early adulthood: increased familial loading and specificity. Archives of General Psychiatry 41, 1136-1143.

Wing, J.K., Babor, T., Brugha, T., Burke, J., Cooper, J.E., Giel, R., Jablenski, A., Regier, D., Sartorius, N., 1990. SCAN. Schedules for Clinical Assessment in Neuropsychiatry. Archives of General Psychiatry 47, 589-593.

Figure 1: Parent depression symptoms over time according to class

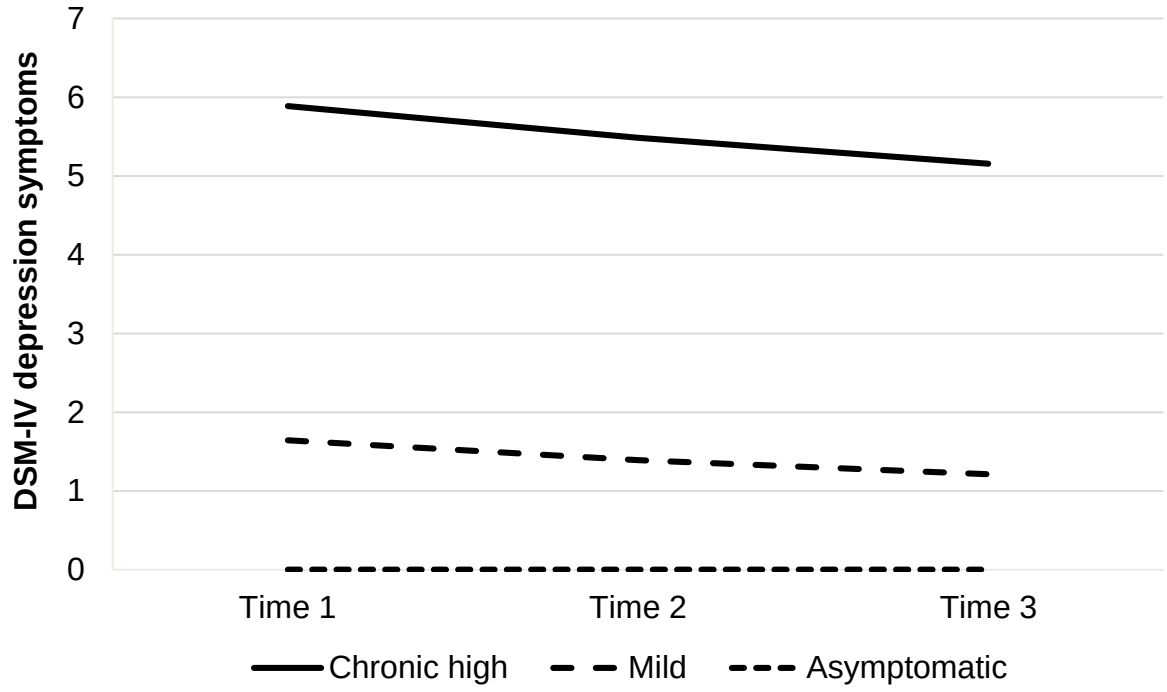

Table 1: Parent and offspring demographic information (n=233)

	Time 1	Time 2	Time 3
Index parent and offspring age and gender			
Parent female gender, n (%)	214 (91.85%)	-	-
Parent age, mean (SD)	42.16 (5.39%)	43.55 (5.40%)	44.60 (5.41%)
Child female gender, n (%)	133 (57.1%)	-	-
Child age, mean (SD)	12.33 (1.98)	13.73 (2.01%)	14.78 (2.01%)
Parent depression			
Diagnosis of MDD	52 (22.4%)	45 (19.5%)	40 (17.2%)
DSM-IV depression symptoms, mean (SD)	2.38 (2.61)	2.06 (2.54)	1.89 (2.43)
Offspring DSM-IV psychiatric disorder			
Any disorder	52 (22.3%)	62 (26.8%)	58 (24.9%)
Any mood disorder	10 (4.29%)	23 (9.96%)	22 (9.44%)
Any anxiety disorder	27 (11.6%)	28 (12.1%)	32 (13.7%)
Any disruptive behaviour disorder	12 (5.2%)	23 (10.0%)	19 (8.2%)
Child depression symptoms, mean (SD)	1.60 (1.83)	1.85 (1.90)	1.93 (2.04)

Any DSM-IV disorder includes all assessed DSM-IV disorders apart from specific phobia; mood disorders include major depressive disorder, dysthymia, depressive disorder not otherwise specified, adjustment disorder with depressed mood, bipolar spectrum disorder and cyclothymia; anxiety disorders include generalised anxiety disorder, separation anxiety disorder, obsessional compulsive disorder, panic disorder, agoraphobia, social phobia, anxiety disorder not otherwise specified and adjustment disorder with anxiety; disruptive behaviour disorders include oppositional defiant disorder, conduct disorder and disruptive behaviour disorder not otherwise specified

Table 2: Parent and offspring demographic information according to parent depression symptom class

Sample demographics at baseline	Asymptomatic class	Mild symptoms class	Chronic high symptoms class	P value
Parent age, mean	43.3	42.0	42.0	0.398
Child age, mean	11.8	12.4	12.4	0.336
Child gender, % female	67.9%	51.5%	68.7%	0.135

Table 3: Differences in clinical depression features and impairment according to parent depression symptom class

	Parent depression symptom class	%/mean (SE)	Difference [95% CI]	Omnibus P value
Parent clinical depression features				
Age of depression onset, years (mean)	Asymptomatic class	30.7 (1.7)	(ref)	0.001
	Mild symptoms class	26.5 (0.7)	-4.2 [-7.88 to -0.52]	
	Chronic high symptoms class	22.3 (1.5)	-8.38 [-12.89 to -3.86]	
Severe depression (% GAF <30 or hospitalisation)	Asymptomatic class	12.6 (8.5)	(ref)	0.003
	Mild symptoms class	23.7 (3.7)	11.1 [-7.07 to 29.27	
	Chronic high symptoms class	49.0 (7.8)	36.4 [13.79 to 59.01]	
Medication taken during study (%)	Asymptomatic class	49.3 (11.6)	(ref)	0.009
	Mild symptoms class	70.0 (3.9)	20.7 [-3.29 to 44.69]	
	Chronic high symptoms class	89.3 (5.1)	40.0 [15.16 to 64.84]	
Psychological treatment during study (%)	Asymptomatic class	3.4 (6.4)	(ref)	<0.001
	Mild symptoms class	19.0 (3.4)	15.6 [1.40 to 29.80]	
	Chronic high symptoms class	49.4 (7.8)	46.0 [26.22 to 65.78]	
Parent impairment *				
Quality of life (health-related): EuroQol, time 3[a] (mean)	Asymptomatic class	0.5 (0.2)	(ref)	<0.001
	Mild symptoms class	0.7 (0.1)	0.2 [-0.18 to 0.59]	
	Chronic high symptoms class	2.9 (0.4)	2.4 [1.55 to 3.28]	
Social impairment: Unemployment of index parent, time 3 (%)	Asymptomatic class	7.8 (7.5)	(ref)	<0.001
	Mild symptoms class	18.0 (3.4)	10.2 [-5.94 to 26.34]	
	Chronic high symptoms class	49.8 (7.8)	42.0 [20.79 to 63.21]	

[a] *The EuroQol does not include the depression/anxiety score*

* *There was little attenuation in results following adjustment for child age and sex*

Table 4: Differences in prevalence of offspring DSM-IV psychiatric disorder according to parent depression symptom class

Offspring disorder	Parent depression symptom class	% (SE)	Risk difference [95% CI]	Omnibus P value
Any DSM-IV psychiatric disorder	Asymptomatic class	5.7 (9.5)	(ref)	0.050
	Mild symptoms class	40.2 (4.3)	34.5 [14.06 to 54.94]	
	Chronic high symptoms class	57.4 (7.5)	51.7 [27.98 to 54.94]	
Any mood disorder	Asymptomatic class	1.6 (5.4)	(ref)	0.002
	Mild symptoms class	14.3 (3.0)	12.7 [0.59 to 24.81]	
	Chronic high symptoms class	37.7 (7.5)	36.1 [17.99 to 54.21]	
Any disruptive behaviour disorder	Asymptomatic class	4.5 (6.4)	(ref)	0.438
	Mild symptoms class	16.1 (3.2)	11.6 [-2.42 to 25.62]	
	Chronic high symptoms class	21.4 (6.5)	16.9 [-0.98 to 34.78]	
Any anxiety disorder	Asymptomatic class	8.7 (8.0)	(ref)	0.052
	Mild symptoms class	24.3 (3.6)	15.6 [-1.59 to 32.79]	
	Chronic high symptoms class	40.0 (7.8)	31.3 [9.40 to 53.20]	

There was little attenuation in results following adjustment for child age and sex

Any DSM-IV disorder include all assessed DSM-IV disorders apart from specific phobia; mood disorders include major depressive disorder, dysthymia, depressive disorder not otherwise specified, adjustment disorder with depressed mood, bipolar spectrum disorder and cyclothymia; anxiety disorders include generalised anxiety disorder, separation anxiety disorder, obsessional compulsive disorder, panic disorder, agoraphobia, social phobia, anxiety disorder not otherwise specified and adjustment disorder with anxiety; disruptive behaviour disorders include oppositional defiant disorder, conduct disorder and disruptive behaviour disorder not otherwise specified

Table 5: Differences in the mean number of offspring DSM-IV depression symptoms according to parent depression symptom class

	Parent depression symptom class	Mean (SE)	Difference in means [95% CI]	Omnibus P value
DSM-IV depression symptoms at time three	Asymptomatic class Mild symptoms class Chronic high symptoms class	0.99 (0.24) 1.92 (0.17) 2.50 (0.38)	ref 0.93 [0.36 to 1.50] 1.51 [0.64 to 2.38]	<0.001

There was little attenuation in results following adjustment for child age and sex